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Hemodialysis Care Staff Perceptions on Barriers to Optimal Health: Results from a Qualitative Study and National Survey

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To the Dean of the Graduate School:

We are submitting a thesis written by Daniela A. Gutierrez More entitled Hemodialysis care staff perceptions on barriers to optimal health: Results from a qualitative study and national survey. We recommend acceptance in partial fulfillment of the requirements for the degree of Master of Science in Human Nutrition.*

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*Master of Science in Human Nutrition

**Winthrop University

HEMODIALYSIS CARE STAFF PERCEPTIONS ON BARRIERS TO OPTIMAL HEALTH: RESULTS FROM A QUALITATIVE STUDY AND NATIONAL SURVEY

A Thesis

Presented to the Faculty

Of the College of Arts and Sciences

In Partial Fulfillment

Of the

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By

Daniela A. Gutierrez More

ABSTRACT

Chronic Kidney Disease (CKD) is currently the ninth leading cause of death in the United States, and despite the favorable outcomes reported in previous studies, mortality rates for CKD have yet to show improvement. The purpose of this study was distinguish between the different strategies used to treat CKD as perceived by renal practitioners. It is hypothesized that the lack of improvement in mortality rates may be attributed to the lack of cardiovascular protection.

This study was a descriptive qualitative study conducted from February 5th, 2019 to March 21st, 2019, following the completion of a pilot study. Participants completed a survey with questions related to their experience working with CKD patients and the current nutrition education provided to patients at dialysis units. In this study, renal practitioners from 250 dialysis units in continental states of the United States were contacted to gather information on their perspectives in relation to nutrition education in dialysis units. The sample included registered dietitians (n=63), registered nurses (n=3) and certified nurse assistants (n=2). The original sample consisted 76 participants, of which 68 met the criteria of: currently working with dialysis patients and not have participated in the pilot study. Descriptive data was analyzed using software Minitab and Microsoft Excel was used to create visual representation of the responses.

Findings suggest that there is indeed a lack of focus on the quality over quantity of nutrients when providing nutrition education to CKD dialysis patients and this may

translate into the negative outcomes commonly observed in relation to cardiovascular health and subsequent mortality rates in the CKD population. Current guidelines are targeting the state of uremia in dialysis patients, putting a larger emphasis on the quantity rather than the quality of nutrients, contributing to a harmful state for these patients' cardiovascular system.

To my grandmother and best friend; both who cheer me on from heaven.

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I would like to acknowledge my husband and son for supporting me with love and patience; my parents and siblings for their time and understanding; and my committee members, who provided me guidance through this academic achievement.

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CHAPTER I

INTRODUCTION

Statement of the Problem

The obesity pandemic has brought an increased prevalence of chronic diseases, such as type II diabetes mellitus and hypertension, which are the most common causes of chronic kidney disease (CKD) (Hruby & Hu, 2015; Hossain, Kawar, & El Nahas, 2007; Hurt, Kulisek, Buchanan, & McClave, 2010; Mitchell, Catenacci, Wyatt, & Hill, 2011). A healthy kidney is able to remove all metabolic by-products via urine and it also participates in hormone production, maintaining the state of homeostasis in the body. When kidneys are damaged, toxins begin to build up due to the inability to effectively filter the blood, causing further decline in kidney function. Kidney disease, which represents the ninth leading cause of death in the US (Xu, Murphy, Kochanek, & Bastian, 2018), is a degenerative condition characterized by a gradual decline in kidney function and structural changes; when these abnormalities in function and structure persist for longer than three months, this disease is classified as CKD (Kidney Disease Improving Global Outcomes, 2013). Chronic kidney disease is asymptomatic, thus early screening and detection, as well as adherence to prescribed interventions, are the most effective ways of slowing or avoiding the progression of the disease (National Kidney Foundation, 2019b).

Uremia is a condition characterized by abnormal levels of waste products in the blood. Many of the complications experienced by the CKD population are

attributed to occurrence of uremia (Meyer & Hostetter, 2014). Dialysis is unable to remove retained waste products as effectively as healthy kidneys would, therefore current nutritional guidelines for CKD are focused on improving the state of uremia observed in individuals with CKD. However, current guidelines are not effective at providing the cardiovascular protection this population is in desperate need for, as they focus more on restrictions of specific nutrients as opposed to the potential impact of quality over quantity of nutrients consumed.

The screening process for CKD includes identifying high-risk patients, such as those with Type 1 or 2 Diabetes Mellitus, hypertension, cardiovascular disease and/or with a family history of CKD, and followed by assessing urinary albumin excretion and calculating estimated glomerular filtration rate (eGFR) from stable serum creatinine levels. Estimated GFR can be calculated using either the Modification of Diet in Renal Disease (MDRD) Study Equation or the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (Levey et al., 2009; Stevens et al., 2007). Other labs used to confirm CKD diagnosis are blood urea nitrogen (BUN), hematocrit and hemoglobin. BUN measures the amount of waste products in the urine, in the form nitrogen and urea. Nitrogen is a by-product of protein metabolism, and urea is a waste product formed by the liver from available ammonia and carried by the blood to the kidneys for excretion. Hematocrit is measured to determine the proportion of the blood that consists of red blood cells. Hemoglobin is measured to check on the production of erythropoietin (EPO) hormone. EPO is secreted by the kidneys in response to low oxygen in order to stimulate red blood cell production. The

intervention prescribed following a CKD diagnosis depends on the severity of the disease at the time of detection but it generally includes diet modification, prescription of pharmaceuticals and at later stages, dialysis or kidney transplantation.

Regardless of etiology, the loss of kidney function in CKD disrupts homeostasis in the body. The albumin creatinine ratio (ACR) and the eGFR are mechanisms used to grade the stage of CKD. Albumin is a protein normally found in the blood and creatinine is the product of muscle metabolism. ACR varies among the stages of CKD. Estimated GFR is a measure used to describe the flow rate of filtered fluid through the kidney. Normal kidney function is characterized as an eGFR $\geq$90 mL/min/1.73m^2. Individuals with normal GFR but with another indicator of kidney damage are diagnosed as stage one. Stages 2 through 5 are diagnosed based on eGFR, as summarized in Table 1. When the eGFR is less than 60 mL/min/1.73 m^2, certain disruptions in homeostasis begin to occur. Phosphorus retention occurs due to reduced urinary phosphorus excretion. This results in decreases in serum calcium levels due to the binding of phosphorus to calcium. To return to homeostasis, the parathyroid gland releases parathyroid hormone (PTH) which releases calcium from bone and stimulates renal tubule reabsorption of calcium. PTH also decreases renal phosphorus reabsorption and increases excretion. Thus, serum calcium and phosphorus return to normal at the expense of a higher serum PTH. With every decrease in eGFR, the process repeats itself. Eventually the eGFR gets so low that hyperphosphatemia impairs gut absorption of calcium leading to hypocalcemia, while PTH continues to rise (Martin & Gonzalez, 2007).

Table 1. Stages of CKD

Stages of CKD		GFR (mL/min/1.73m^2)
Stage 1	Kidney damage with normal kidney function	≥90
Stage 2	Kidney damage with mild loss of kidney function	60 – 89
Stage 3	Moderate loss of kidney function	30-59
Stage 4	Severe loss of kidney function	15-29
Stage 5	Kidney failure, or ESRD	<15

Increased serum phosphorus also suppresses the synthesis of $1,25(OH)_2$ vitamin D_3, which in turn decreases bone formation. Increased PTH, while bad for bone, will stimulate synthesis of $1,25(OH)_2$ vitamin D_3 by the failing kidneys in an attempt to normalize secretions. Metabolic acidosis develops because the failing kidneys cannot keep up with the excretion of the metabolically generated hydrogen ions. The excess hydrogen ions are buffered by bicarbonate, but they also make their way into bone cells causing the release of calcium ions, weakening bone even more. Thus, the combination of bone reabsorption from too much PTH, the buffering of hydrogen ions, and the decreased bone formation due to low $1,25(OH)_2$ vitamin D_3, results in the development of renal osteodystrophy, the bone malformation aspect of CKD-Mineral and Bone Disorder (CKD-MBD) (Martin & Gonzalez, 2007).

It is known that when calcium-phosphorus product exceeds the solubility product, it may contribute to crystal precipitation in the vasculature (Yamada & Giachelli, 2016). However, klotho and FGF23 are also thought to play a key role in vascular calcification. There is growing evidence gathered from animal experiments that demonstrates that a decrease in klotho levels can cause vascular calcification, cardiac hypertrophy, cardiac fibrosis (Lu & Hu, 2016). The changes in metabolic pathways of bone minerals, the interruption in calcium and phosphate homeostasis, and the vascular calcification observed in CKD patients in relation to these alterations are collectively known as CKD-MBD (Kidney Disease Improving Global Outcomes, 2017).

Mineral and bone disorders are an inevitable consequence of CKD. While many approaches are taken to treat CKD-MBD, no data currently exists stating its exact prevalence. Research has shown that intervention in the form of intense nutrition education can significantly improve clinical outcomes as well as improve quality of life (Duff & Chawke, 2017; Ebrahimi, Sadeghi, Amanpour, & Dadgari, 2016; Karavetian, de Vries, Elzein, Rizk, & Bechwaty, 2015; Karavetian, Elzein, Rizk, Jibai, & De Vries, 2016).

Specific Aims

The focus of this thesis is to distinguish between the different strategies used to treat Chronic Kidney Disease- Mineral Bone Disorder, the perceptions across

disciplines and barriers to maintaining mineral homeostasis during dialysis. The specific aims for this study are:

Aim 1: To explore the current barriers perceived by renal practitioners at dialysis units when addressing the imbalance of minerals that manifests as a result of CKD.

Aim 2: To identify the nutrition education techniques that are used most frequently in dialysis units and the main concepts discussed in reference to bone mineral metabolism.

Aim 3: To understand what specific nutrients healthcare practitioners target when providing nutrition education to manage CKD-MBD.

Aim 4: To determine the amount of time that is being devoted to nutrition education by different renal practitioners and to distinguish how nutrition information is being delivered across disciplines.

CHAPTER II

LITERATURE REVIEW

Epidemiology of Chronic Kidney Disease

Prevalence and stages of chronic kidney disease

Approximately 37 million American adults suffer from chronic kidney disease (CKD). The national prevalence for chronic kidney disease stages 1-4 is estimated to be 15% according to data from 2013–2016 National Health and Nutrition Examination Survey (NHANES). It is estimated that one in two people with severely decreased kidney function and 96% of people with kidney damage or mild loss of kidney function are undiagnosed, while many others are unaware of their increased risk for this disease (Center for Disease Control and Prevention, 2017; 2019). Data from NHANES 1999-2014 indicate that about 2.7% of individuals diagnosed with kidney disease reported being aware of their condition in 2012, and about 2.8% in 2014. If left untreated, kidney disease can lead to death. As of 2016, this progressive and chronic condition reported a national death rate of 13.1 per 1000 deaths (Center for Disease Control and Prevention, 2018).

The estimated glomerular filtration rate (eGFR) measurement is used to evaluate kidney function and is calculated by using a GFR estimating equation to derive eGFR from serum creatinine ($eGFR_{Cr}$). (Kidney Disease Improving Global Outcomes, 2013; Levey et al., 2009; Stevens et al., 2007). The most commonly used GFR estimating equations are Modification of Diet in Renal Disease (MDRD) Study

Equation or the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (Table 2) (Levey et al., 2009; Stevens et al., 2007).

Table 2. Glomerular filtration rate equations

MDMR	eGFR (ml/min/1.73m^2) = 175 x $(S_{cr})^{-1.154}$ x $(Age)^{-0.203}$ x (0.742 if female) x (1.212 if African American)
CKD-EPI creatinine	eGFR (ml/min/1.73m^2) = 141 x min $(S_{cr}/k, 1)^{\alpha}$ x max $(S_{cr}/k, 1)^{-1.209}$ x 0.993^{Age} x (1.018 if female) x (1.159 if African American)
CKD-EPI Cystatin	eGFR (ml/min/1.73m^2) = 133 x min $(S_{cys}/0.8, 1)^{-0.499}$ x max $(S_{cys}/0.8, 1)^{-1.328}$ x 0.996^{Age} x (0.932 if female)

S_{cr} (standardized serum creatinine) = mg/l
S_{cys} (standardized serum cystatin C) = mg/l
k is 0.7 for females and 0.9 for males,
α is -0.329 for females and -0.411 for males

Current guidelines favor the use of the CKD-EPI equation as current evidence has shown increased accuracy, particularly at higher GFR (Kidney Disease Improving Global Outcomes, 2013). Evidence also shows that estimating GFR from cystatin C ($eGFR_{Cys}$) instead of serum creatinine can be a more powerful indicator of GFR, yet there is a lack of evidence showing that the favorable outcomes of using this expensive method outweighs the burden of cost (Florkowski & Chew-harris, 2011). Current guidelines recommend using $eGFR_{Cys}$ only in cases where cystatin C has being measured or when required as a confirmatory test for patients found to have $eGFR_{Cr}$ of 45-59 ml/min per 1.73m^2 but absent of any other indicator of kidney

damage (Kidney Disease Improving Global Outcomes, 2013). Recent studies are exploring the effectiveness of new GFR estimating equations, such as the Lund-Malmo equation or Full- Age Spectrum equation, but their use has not yet being validated to replace current recommendations (Nyman et al., 2014; Pottel et al., 2016).

Once GFR has been determined, the measurement of eGFR is used to classify the severity of the loss of kidney function is categorized into five stagesas summarized in Table 1. Individuals are considered to have reduced kidney function when diagnosed as stage 3 and often require the use of renal replacement therapy (RRT), or dialysis, to mimic the blood filtering functions of the kidneys when stage five is reached (Kidney Disease Improving Global Outcomes, 2013).

Another important measurement used to confirm the diagnosis of kidney disease by assessing kidney damage is the albumin to creatinine ratio (ACR). Albumin is a protein normally found in the blood. When kidneys are healthy, this macromolecule is unable to pass into the urine. When there is kidney damage, the glomerular permeability is altered resulting in abnormal urinary protein excretion and accumulation of waste products in the blood. For example, creatinine, a waste product of muscle metabolism, is filtered effectively by a healthy kidney but not when kidney damage is noted. Persistent protein leakage is associated with increased risk of CKD progression (Cravedi & Remuzzi, 2013). The ACR measurement assesses the urinary albumin excretion and it is used for the classification of three albuminuria categories: <30 mg/g classified as mild, 30-300 mg/g as moderate, and >300 mg/g as severe

(Kidney Disease Improving Global Outcomes, 2017). KDIGO 2012 guidelines recommend that CKD should be classified based on etiology, stages of GFR and categories of albuminuria. The nutrition and medical intervention vary in accordance to the stages (Kidney Disease Improving Global Outcomes, 2013).

Unfortunately, although kidney transplant is an option for patients with ESRD, not all ESRD patients are suitable candidates for transplantation. Healthcare practitioners discuss eligibility with patients and educate them about renal transplantation when they are approaching ESRD or in some instances, are already at this stage. The availability of the use of transplantation as a kidney replacement therapy is determined by the perceived risks of transplantation relative to the risks of not receiving a transplant. Some of the factors to be considered are age, psychosocial status, weight status, perceived adherence and tobacco use ("KDIGO Clinical Practice Guideline on the Evaluation and Management of Candidates for Kidney Transplantation Public Review Draft," 2018).

Risk factors and comorbidities of chronic kidney disease

Risk factors for CKD can be categorized into two groups: modifiable risk factors (such as lack of physical activity, poor diet, tobacco use, exposure to toxic substances and obesity), and non-modifiable (such as age, gender, low-birth weight, genetics, socioeconomic status and family history). Conditions such as diabetes mellitus (Type 1 and 2) and hypertension result in an increase in risk for developing CKD. The risk for developing ESRD increases by 12-fold in diabetics and 7-fold in

hypertensive patients (Kazancioğlu, 2013). In addition, not only is obesity a risk factor for CKD, but also for diabetes, hypertension, and cardiovascular diseases (Kazancioğlu, 2013). Findings suggests that obesity has an impact in the pathogenesis of CKD regardless of the presence of diabetes mellitus and/or hypertension (Garland, 2014). The growing concern for rapidly increasing rates of chronic disease such as CKD, diabetes and hypertension is, in part, associated with the recent rise in obesity rates (Hruby & Hu, 2015; Hossain, Kawar, & El Nahas, 2007; Hurt, Kulisek, Buchanan, & McClave, 2010; Mitchell, Catenacci, Wyatt, & Hill, 2011).

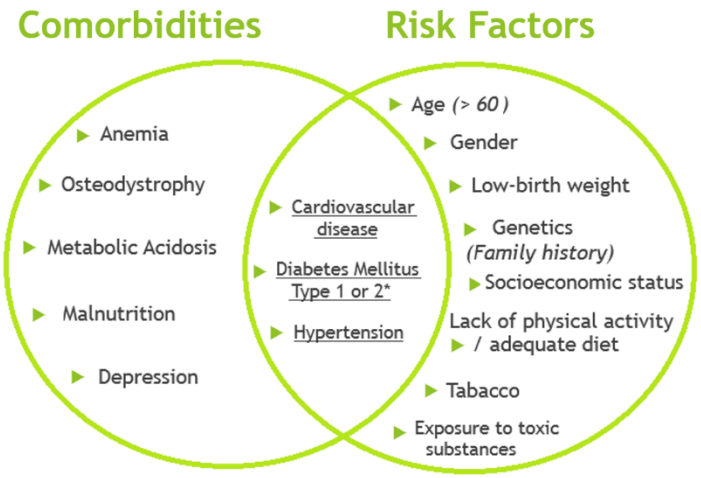

Figure 1. Comorbidities versus risk factors for CKD

Diabetes Mellitus Type 1 and Type 2 not only represent strong risk factors for CKD but they are also conditions commonly found to coexist with CKD. A report released by the Centers for Disease Control and Prevention (CDC) in 2015 estimates that about 30.3 million Americans (about 9.4% of the US population) have diabetes

and 84.1 million have pre-diabetes, a condition that acts as a precursor for Type 2 diabetes mellitus. National Health and Nutrition Examination Survey (NHANES) data from 1999-2006 demonstrated that approximately 39.6% of people with diagnosed diabetes suffer from CKD, in contrast to 41.7% with undiagnosed diabetes, 17.7% with prediabetes and 10.6% of people without diabetes (Plantinga et al., 2010).

Hypertension, a condition characterized by elevated blood pressure, also represents a strong risk factor and common coexisting condition for CKD. According to the CDC, about one in every three adults in the United States suffer from high blood pressure and only about half of them have their condition under control (Center for Disease Control and Prevention, 2016; Nwankwo, Yoon, Burt, & Gu, 2013). In 2013-2014 the prevalence for self-reported hypertension in CKD population was reported to be 59.1% (Center for Disease Control and Prevention, n.d.). Uncontrolled hypertension represents a risk factor for CKD and can also accelerate the deterioration of kidney function; concurrently, CKD is also found to be a risk factor for hypertension due to the effect of the decline in kidney function in blood pressure levels (Judd & Calhoun, 2015). Blood pressure is poorly controlled by individuals with CKD, despite of the growing evidence on the effects of uncontrolled blood pressure in the progression of CKD (Lee et al., 2017). The U.S. Renal Data System (USRDS 2002) reported that CKD patients are more likely to die than to reach end-stage renal disease (ESRD), and majority of those deaths are attributed to cardiovascular complications (Snyder, J.J., & Collins, 2017; *U.S. Renal Data System: USRDS 2002 Annual Data Report, Bethesda MD*, 2002).

In spite of hypertension and diabetes mellitus being the major correlates to CKD, there are other important risk factors to consider. CKD has been linked to genetic and environmental factors such as genetic composition, family history, gender, acute kidney injury and toxins. A study conducted by Kottgen et al. (2009) explored the association between genetics and the pathogenesis of kidney disease. Results suggested that genetics can increase the susceptibility for decreased kidney function by passing down mutations, or errors, in the gene code affecting the process by which Tamm-Horsfall proteins are made within the kidneys. However, there is a need for further research in the area of genetics to provide a better understanding of the genetic component of CKD.

Susceptibility to developing CKD is not only thought to be affected by genetics, but also by family history, age and gender. CKD is hereditary, hence the importance of family history when dealing with this population. Chances of having CKD also increase with age over 60. A study by Suleymanlar et al. (2011) conducted in Turkey reported the odds ratios of CKD as 1.45-2.18 for every 10 year increase in age and reported the CKD odds ratios as 1.54 for females over males (Süleymanlar et al., 2011). According to the CDC, CKD is more prevalent in females than males (16% vs 13%), but males are 64% more likely than females to develop ESRD (Center for Disease Control and Prevention, 2017). This statement is corroborated with an article by Goldberg, and Krause in which the researchers explain the differences in progression of the disease among genders and states that despite the increased prevalence of CKD for women, CKD in men tends to progress more rapidly giving

males a higher prevalence for ESRD as well as mortality rate from this condition (Goldberg & Krause, 2016). Physical injuries, infections, drugs or toxins are all capable of injuring the kidneys and speed up the disease if already present (Center for Disease Control and Prevention, 2017).

Another comorbidity of CKD is anemia. One of the primary causes may be the amount of iron lost during hemodialysis (Besarab & Ayyoub, 2007) . The prevalence for anemia in patients with CKD is estimated to be approximately 8.4% in stage 1 up to the rate of 53.4% in stage 5. Prevalence of anemia among people without CKD is approximately 6.3% (Stauffer & Fan, 2014). Another factor contributing to anemia in this population is the diminished erythropoiesis resulting from kidney damage. Erythropoietin is a hormone secreted by the kidneys in response to a low oxygen level in order to stimulate red blood cell production. Kidney damage compromises the production of erythropoietin and can contribute to the anemia in chronic kidney disease (Stauffer & Fan, 2014). An imbalance in iron homeostasis also contributes to the manifestation of anemia in CKD. This imbalance is partly due to the increased iron losses resulting from dialysis and the abnormal levels of hepcidin hormone secretion. Hepcidin is a hormone secreted by the liver and its main function is to maintain systemic iron homeostasis. It does this by binding an inducing degradation ferroportin (an iron exporter) on duodenal enterocytes, reticuloendothelial macrophages, and hepatocytes to inhibit iron entry into the plasma. Data suggests that the excess hepcidin observed in CKD patients may contribute to the impaired dietary iron absorption and reticuloendothelial cell iron blockade in this population (Babitt & Lin,

2010; Courselaud et al., 2002; Krause et al., 2000; Nemeth et al., 2004; Park, Valore, Waring, & Ganz, 2001). Course of treatment for anemia in CKD population include iron supplementation, erythropoietin stimulating agents or even blood transfusions (Lawler et al., 2010; Stauffer & Fan, 2014). Results from a retrospective cohort study suggest that patients are more likely to initiate iron supplementation therapy (30.8%) and blood transfusion (16.1%) than they are to receive erythropoietin stimulating agents (7.1%) (Lawler et al., 2010). Despite the etiology, implementing proper screening techniques for identifying individuals at risk for CKD can result in prevention or delayed progression of CKD and its comorbidities.

Chronic Kidney Disease-Mineral and Bone Disorder

Pathophysiology of chronic kidney disease-mineral bone disorder

Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD) is characterized by disturbances in mineral and bone metabolism. This includes abnormalities in the metabolism of calcium, phosphorus, parathyroid hormone (PTH), and vitamin D. This can lead to abnormalities in bone turnover, mineralization, volume, linear growth, strength and calcification of vascular or other soft tissue (Kidney Disease Improving Global Outcomes, 2017). The progressive calcitriol ($1,25(OH)_2$ vitamin D_3) deficiency that is often manifested by Stage 2 of CKD was thought to be the first clinical indicator of Mineral Bone Disease (Levin et al., 2007). Current research suggests that the pathophysiology of CKD-MBD begins with alterations of the hormone Fibroblast Growth Factor-23 (FGF-23) and its co-receptor

α-klotho which occur prior to the decrease in serum active vitamin D levels. FGF23 is a hormone synthesized by osteocytes and osteoblasts (bone cells). Findings suggest that FGF-23 could be a potential cause of the CKD associated vitamin D deficiency by suppressing renal 1α-hydroxylase expression in proximal tubules. 1α-hydroxylase is an enzyme that catalyzes the activation of 25-hydroxyvitamin D to $1,25(OH)_2$ vitamin D_3 (Hruska, Seifert, & Sugatani, 2016).

The Chronic Renal Insufficiency Cohort study had similar findings about the way FGF23 suppresses 1α-hydroxylase leading to vitamin D deficiency observed in early stages of CKD (Isakova et al., 2011). The resulting low levels of $1,25\ (OH)_2$ vitamin D_3 from over production of FGF23 affects parathyroid hormone (PTH) secretion. Low levels of vitamin D lead to the inability to obtain the proper amount of calcium from their diet by decreasing its gastrointestinal (GI) absorption, and also an increase in PTH secretion in an attempt to increase calcium levels. Elevated PTH levels will promote vitamin D activation in the proximal tubules of the kidneys and osteoclast differentiation and bone resorption, mobilizing calcium (along with phosphorus) from the bones (Figure 1). PTH will also increase calcium resorption in the GI tract. In spite of this indirect relationship between FGF23 and increased PTH secretion, there is a feedback loop representing a direct connection between FGF23 and PTH. The production of FGF23 acts like a brake pedal by directly decreasing PTH synthesis and secretion in the parathyroid gland (Komaba & Fukagawa, 2010).

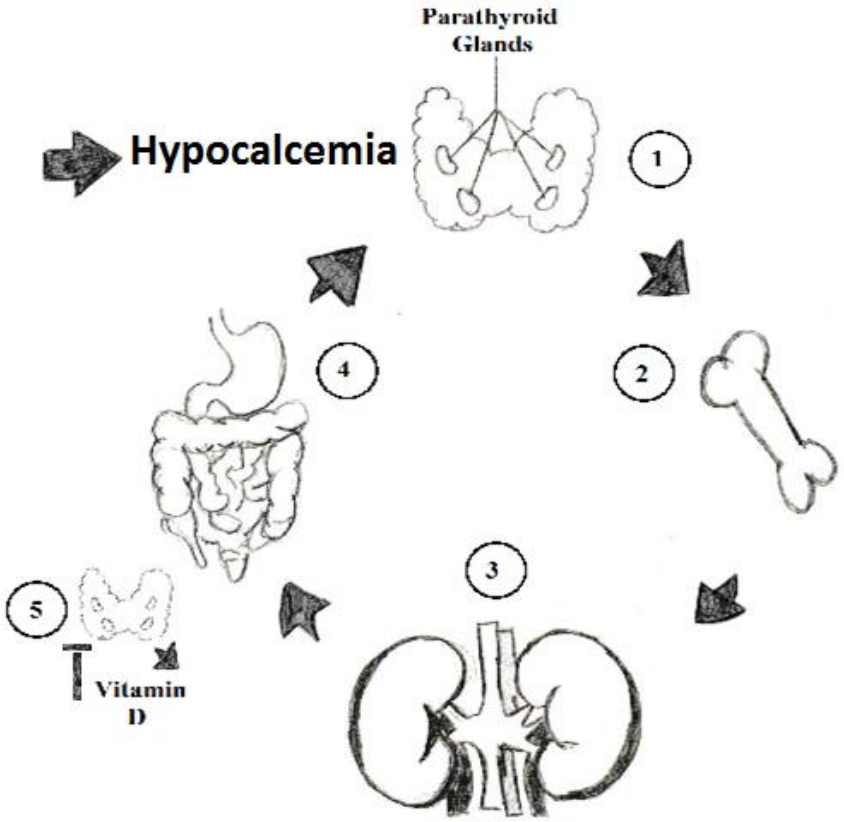

Figure 2. Metabolic changes in state of hypocalcemia

1) The parathyroid gland protects the body against hypocalcemia by constantly regulating serum calcium levels. In state of hypocalcemia, the parathyroid releases parathyroid hormone (PTH) and additional PTH is synthesized 2) PTH acts on the bones and mobilizes calcium to increase serum calcium levels 3) PTH stimulates calcium resorption and vitamin D activation in the kidneys 4) Released vitamin D then facilitates calcium resorption in the gastrointestinal tract (GI) 5) Endocrine feedback loop: PTH drives the activation of vitamin D, and the active vitamin D then shuts off PTH production.

FGF23 is synthesized in response to elevated phosphate levels leading to increased phosphorus excretion and decreased GI absorption (Hruska et al., 2016). As a result to this previously explained mechanisms, phosphorus and PTH levels remain

normal until later stages of the disease. α-Klotho acts as a cofactor in the regulation of FGF23 signaling, thus working together in the pathway to provide mineral ion homeostasis. As the disease progresses, klotho deficiency develops and this not only leads to hyperphosphatemia but it also deactivates the feedback loop with the parathyroid gland that brakes the production of PTH, therefore leading to overproduction of PTH and increased calcium and phosphorus excretion from the bones (Hruska et al., 2016).

Another factor that is involved in the progression of CKD is high phosphorus consumption (Figure 2). In rodents, increased renal tubular damage is positively associated with increased phosphate excretion (Haut et al. 1980). A retrospective cohort study by Kawasaki (2015) explored this association by evaluating the effects of increased phosphorus consumption on each nephron. Researchers measured urinary phosphorus excretion per creatinine clearance and concluded that there was indeed an association between higher levels of phosphorus excretion per creatinine clearance and the progression of CKD. This lead to the idea that although phosphorus levels are not increased during early stages of CKD, high phosphorus consumption results in more phosphorus to be excreted. This results in higher level of renal tubular damage due to added burden on each nephron (Kawasaki et al., 2015).

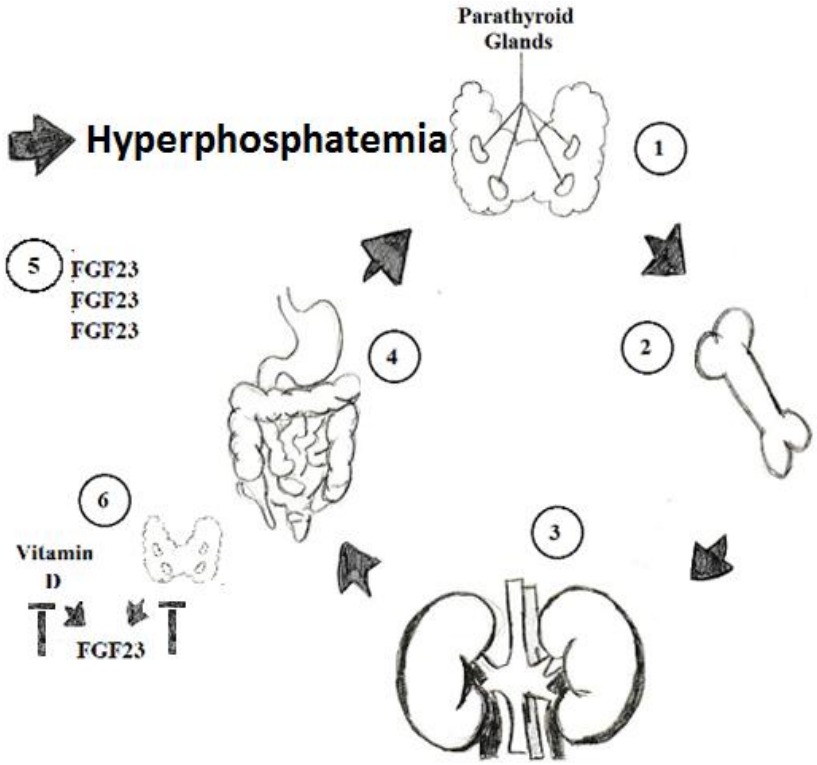

Figure 3. Metabolic changes in state of hyperphosphatemia

1) The parathyroid gland releases parathyroid hormone (PTH) in response to elevated serum phosphorus levels 2) PTH acts on the bones and mobilizes phosphorus, therefore increasing serum levels 3) PTH stimulates vitamin D activation in the kidneys and increases phosphorus excretion 4) Released vitamin D then increases phosphorus reabsorption in the gastrointestinal tract (GI tract) 5) Fibroblast growth factor 23 (FGF23) is triggered by high phosphorus, PTH and active vitamin D levels. FGF23 increases phosphorus excretion and blocks activation of vitamin D leading to decreased levels of active vitamin D and a subsequent decrease in GI absorption of phosphorus. More phosphorus in then excreted in the stool 6) Endocrine feedback loop: Active vitamin D stimulates FGF23 production; FGF23 then serves as a brake pedal for active vitamin D; PTH stimulates FGF23; FGF23 then shuts off PTH production.

Results from a retrospective cohort study concluded that phosphate excess is linked to substantial cardiovascular morbidity and mortality among CKD patients.

This occurs independently from identified confounding factors and is thought to be attributed to the elevated PTH levels, decreased 1,25 $(OH)_2$ vitamin D_3 levels and vascular calcification that results from excessive serum phosphorus levels (Kestenbaum et al., 2005). In this study by Kestenbaum et al. (2005), researchers observed a higher mortality risk among participants with serum phosphorus levels in the high-normal range whereas there was no increase in mortality observed among the participants with lower serum phosphorus levels.

Although high phosphorus intake is not associated with increased mortality rates in moderate kidney disease (Murtaugh et al., 2012), it does increase the rate at which the nephrons deteriorate leading to advanced kidney disease. A cohort study reported similar finding on the deteriorative effects of phosphorus, suggesting that higher dietary phosphorus and phosphorus to protein ratios are linked to increased mortality in hemodialysis patients (Nazanin Noori, Kamyar Kalantar-Zadeh, Csaba P. Kovesdy, Rachelle Bross, Debbie Benner, 2010). Summarizing these studies it becomes evident that mortality due to high phosphorus intake increases as GFR decreases. Ultimately, there is a positive correlation between increased phosphorus intake and rate of progression of CKD due to the high burden put on the nephrons by the increased phosphorus intake.

Fibroblast growth factor 23, klotho and CVD in CKD population

Studies have shown patients with CKD have decreased expression α-klotho (Noritoshi Koh, Toshihiko Fujimori, Shuhei Nishiguchi, Akihiro Tamori, Susumu

Shiomi, Tatsuya Nakatani, Kazunobu Sugimura, Taketoshi Kishimoto, Satoko Kinoshitaa, Tetsuo Kuroki, 2001). Results from a study by Koh et al. (2001) suggest that the decreased expression of α-Klotho in chronic renal failure kidneys is linked to the morphological loss of nephrons seen in the progression of CKD. These alterations result in lower amounts of α-klotho expressing cells in the kidneys as well as the functional deterioration of tubule cells leading to decreased expression of the klotho gene (Noritoshi Koh, Toshihiko Fujimori, Shuhei Nishiguchi, Akihiro Tamori, Susumu Shiomi, Tatsuya Nakatani, Kazunobu Sugimura, Taketoshi Kishimoto, Satoko Kinoshitaa, Tetsuo Kuroki, 2001). As CKD progresses and the expression of α-klotho is decreased, the function of FGF23 is practically abolished, leading to the imbalance in bone mineral metabolism (Figure #).

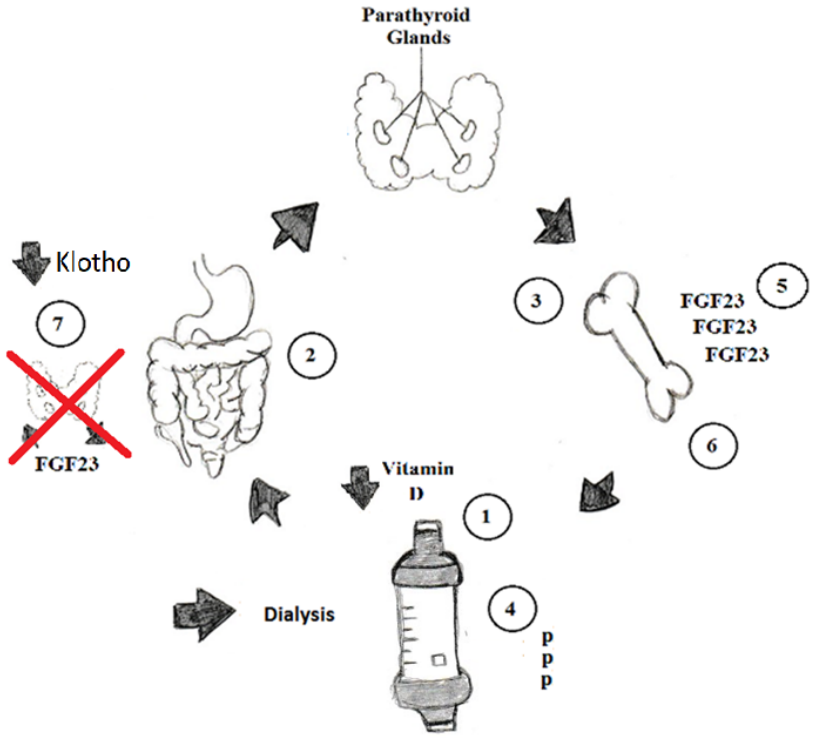

Figure 4. Metabolic changes when kidney tissue is decreased or absent

1) Little to no kidney tissue leads to decreased vitamin D activation 2) decreased levels of vitamin D then cause a decrease in calcium absorption, leading to hypocalcemia 3) hypocalcemia will then act on the bone, mobilizing both calcium and phosphorus 4) taking the kidneys out of the cycle, the counterbalance it provided is now ineffective, leading to persistent hyperphosphatemia 5) this hyperphosphatemia will stimulate PTH production and indirectly call for more FGF23 production 6) FGF23 attempts to get rid of the excess phosphorus thru the urine, but since the kidneys are not viable, this is no longer possible, resulting in persistent FGF23 production 7) Unfortunately, the FGF23 endocrine feedback loop that will normally shut off PTH production is ineffective due to Klotho deficiency

There is a notable increase in risk for cardiovascular disease (CVD) mortality and morbidity in the CKD population (United States Renal Data System, 2018; Yamada & Giachelli, 2016). This population is far more likely to die of CVD than to reach ESRD (Kuro-O, 2011; United States Renal Data System, 2018). The mechanisms involved in the development of CVD within CKD patients goes beyond the traditional risk factors (Yamada & Giachelli, 2016). Novel cardiovascular risk factors include klotho and FGF23. Alpha-Klotho is a gene that acts as a regulator of metabolic processes in the body. Two paralogs of α-klotho have been identified (β-klotho and γ-klotho), yet for the purpose of this paper we will focus on the effects of α-klotho, and hereinafter refer to it as klotho (Lu & Hu, 2016). Klotho gene is found in several organs, but in relation to CKD it is primarily expressed in the kidneys and to a lesser extent in the parathyroid gland and brain (Kuro-o et al., 1997; Lu & Hu, 2016). There are two types of klotho derived from the kL gene, membrane-bound klotho and soluble klotho. There are also two sub-types of soluble klotho, shed and secreted. Shed soluble klotho is derived from the shedding of membrane-bound klotho by ADAM10 and ADAM17 proteases while secreted soluble klotho is derived from an alternative splicing of the membrane-bound klotho (Olejnik, Franczak, Krzywonos-Zawadzka, Kałużna-Oleksy, & Bil-Lula, 2018). The main function of membrane-bound klotho is to act as a co-receptor for FGF-23, a phosphaturic hormone; whereas soluble klotho is involved in anti-aging and the regulation of oxidative stress, inflammation and fibrosis (Olejnik et al., 2018).

FGF23 is a hormone mainly produced by osteocytes and osteoblast. FGF23 promotes phosphate excretion and inhibits vitamin D activation in the kidneys while shutting off PTH production, but it requires the presence of klotho. Unfortunately, klotho levels begin to decline as early as in Stage 1 CKD and continues to decrease as the disease progresses. As klotho deficiency arises, FGF23 production is increased with the attempt to normalize phosphorus levels, yet the resulting inhibition of active vitamin D production reduces klotho expression even further, therefore becoming a cyclic condition (Kuro-O, 2011).

When the calcium-phosphorus product exceeds the solubility product, it may contribute to crystal precipitation in the vasculature (Yamada & Giachelli, 2016). Klotho and FGF23 are also thought to play a key role in vascular calcification. There is growing evidence gathered from animal experiments that demonstrates that a decrease in klotho levels can cause vascular calcification, cardiac hypertrophy, cardiac fibrosis (Lu & Hu, 2016). A study by Chen et al. (2018) examined the mechanism of phosphate-induced calcification in vascular smooth muscle cells and results suggested that klotho and FGF23 have the capability of reversing the calcification induced by high phosphate intake and suppressing phosphate-induced vascular calcification by inhibiting Wnt7b/β-catenin pathway (Chen, Huang, Duan, Xu, & Chen, 2019).

Patients who undergo dialysis show up to a 30-fold increase in cardiovascular mortality in comparison to the general population (Yamada & Giachelli, 2016). Endothelial dysfunction, vascular calcification, oxidative stress and inflammation are

non-traditional risk factors of CKD individuals that are associated with negative cardiovascular outcomes. Studies suggest that the elevated levels of FGF23 is associated with endothelial dysfunction (Yilmaz et al., 2010), and impairment in endothelium-independent vascular function is significantly higher in CKD population in comparison to individuals with CVD but preserved kidney function (Kopel et al., 2017). Researchers concluded that resulting high phosphorus levels speed up the development of CVD in CKD (Prié, Torres, & Friedlander, 2009). To summarize, researchers found that that the imbalance of klotho and FGF23 induces increased rate of progression of CKD and development of CVD in CKD patients. Results suggest that the manifestation of CVD in CKD may be accelerated due to the hyperphosphatemia that ensues (Brancaccio, Bellasi, Cozzolino, & Galassi, 2009).

How impact of diabetes and hypertension affect CKD

CKD is a common microvascular complication of uncontrolled diabetes. Between 25-40% of adults with diabetes develop diabetic nephropathy 20-25 years after the onset of the disease (Kidney Disease Improving Global Outcomes, 2013). Diabetes represents the dominant cause leading to end stage renal disease, (Foley & Collins, 2007) hence the importance of glycemic control in this population to delay or prevent the microvascular complications of diabetes. The mortality rate for this population nearly doubles when these complications arise. KDIGO guidelines (2012) recommend achieving a hemoglobin A1c level of about 7.0% with the purpose of preventing rapid progression microvascular complications, however, it is also

important to identify the potential risk for hypoglycemia (low blood sugar levels) that increases as kidney function declines. Thus, reducing HbA1C further can be counterproductive. KDIGO emphasized that for CKD individuals with reduced red cell lifespan, the HbA1C measurement may not be indicative of glucose control and therefore this biomarker should be interpreted with caution (Kidney Disease Improving Global Outcomes, 2013).

Hypertension is the second leading cause of ESRD in the US. (Rao, Qiu, Wang, & Bakris, 2008). Eighty-five to ninety percent of patients with stage 3-5 CKD suffer from hypertension Aside from being a risk factor for CKD, it also speeds up the progression of the disease (Segura & Ruilope, 2011). Uncontrolled hypertension eventually leads to high intraglomerular pressure, affecting the glomerular filtration rate and causing an increase in protein filtration resulting in a poor prognosis for CKD and cardiovascular disease. According to the KDIGO guidelines, CKD patients should target a blood pressure measurement of less than 130/80 mmHg with the goal of reducing renal and cardiovascular morbidity and mortality. Just as hypertension effects CKD, CKD also has a negative effect on blood pressure. Due to the damaged blood vessels in the kidneys, glomerular filtration is lowered resulting in an increase of fluid volume in the blood leading to hypertension.

Dietary Guidelines and Nutrition Interventions

Dietary guidelines for chronic kidney disease

The Kidney Disease Outcome Quality Initiative (KDOQI) does not have precise recommendation for the early stages of Chronic Kidney Disease. However, the National Kidney Foundation recommends to control the amount of protein, sodium, potassium and phosphorus to avoid buildup of waste and fluid in the blood as well as overworking the kidneys. Current recommendations for adult patients with stage 4 or 5 CKD (GFR < 30 mL/min/1.73m^2) who are not undergoing dialysis include limiting protein intake to 0.6-0.8 g/ per kg of body weight and to avoid intakes of >1.3 grams per kilogram of weight if there is a risk of CKD progression due to proteinuria (Kidney Disease Improving Global Outcomes, 2013). Scientists have had a difficult time providing evidence supporting dietary protein restriction in CKD patients due to lack of patient adherence to low-protein diets. Thus the recommendation for protein limits dietary intake to a similar level as the recommended dietary intake of protein for healthy individuals (Kidney Disease Improving Global Outcomes, 2013). Protein restriction in adults with CKD is thought to help reduce intake of nitrogen, which would put the patient at lower risk of protein waste build-up in the blood, a condition often found in advanced CKD patients. Due to the life stage and the importance of growth at an early age, this protein restriction recommendation only pertains to adults.

Studies exploring the effects of sodium intake (in the form of salt) in CKD progression suggest that high sodium intake induces an increase in proteinuria as well

as a potential decrease in glomerular filtration rate, and an increase in blood pressure (Jones-Burton et al., 2006). Based on this data and the effects of sodium in raising blood pressure (hypertension), KDIGO guidelines recommend that sodium intake is lowered to less than 2 grams/day (equivalent to about 5 grams of sodium chloride). This recommendation, however, may vary based upon the presence of conditions in which salt restriction may be detrimental as opposed to beneficial. For example, salt wasting tubular disorders (Kidney Disease Improving Global Outcomes, 2013).

Dietary guidelines for chronic kidney disease - mineral bone disorder

The increased need for medication to control CKD-MBD parameters may be attributed to the lack of consistency at which this condition is diagnosed. It may also be attributed to the lack of adherence to dietary recommendations by CKD patients. Dietary recommendations focused on the management of chronic kidney disease-mineral bone disorder (for non-dialysis patients) are currently not very specific. Guidelines outline the importance of limiting foods high in sodium, potassium, and phosphorus as well as the consequences of not maintaining these levels as close to normal as possible; however, they do not give precise recommendations for the daily intake of phosphorus and potassium as is the case for protein and sodium (Kidney Disease Improving Global Outcomes, 2017). Isakova and colleagues (2017) published a commentary on the 2017 KDIGO Guidelines in which they suggested the daily intake for phosphorus to be from 0.8-1.0 gram/day and 1 to 2 grams/day for calcium (from all sources), but again there was no concise recommendation given for intake of

potassium. Treatment for mineral and bone disorder is aimed at slowing down the loss of bone (due to renal osteodystrophy) and the elevated amount of minerals deposited in the blood vessels and heart. Current treatments include diet modifications to balance dietary intake with existing kidney function, and medications (Beto, Ramirez, & Bansal, 2014).

Dietary guidelines for CKD and Mineral Bone Disorder at end stage renal disease

When reaching stage five of CKD, many patients undergo renal replacement therapy (RRT), or dialysis. According to the Academy of Nutrition and Dietetics, these patients should modify their protein intake to 1.1-1.5 grams/kilogram of weight due to the amount of protein lost during the RRT process. The bioavailability of the protein is also important to help patients achieve and maintain adequate serum albumin levels. Animal protein has a significantly higher bioavailability in comparison to plant-based proteins, therefore food such as meat, fish, poultry, pork or eggs are encouraged (Linda M. Ulerich, 2019). Sodium recommendation remains the same, limited to about 2-3 grams/day to control fluid gain between dialysis treatments. National Kidney Foundation recommends limiting cured or pickled foods, sauces, salted snacks such as chips or seeds, luncheon meats, processed food and salt seasonings, and flavor enhancers that tend to have a high amount of sodium (National Kidney Foundation, 2019a).

Potassium, calcium, and phosphorus recommendations are more specific once dialysis has begun. Potassium intake is recommended to stay between 2-4 grams /day

or 0.4 grams/kg of body weight/day. Foods such as avocados, potatoes, bananas, and other high potassium foods should be limited, as well as salt substitutes that may include potassium. Phosphorus is recommended to be between 0.8-1 gram/day to achieve normal levels. As previously stated, dialysis patients are often encouraged to increase their animal-based protein due to the increased bioavailability; however, the bioavailability of phosphorus is also higher in animal-based proteins and this should be taken into consideration when educating patients on protein and phosphorus consumption (Moorthi et al., 2014). Bioavailability refers to the degree to which nutrients are available for absorption and utilization. Other than proteins such as meats, nuts, beans and dairy products, dark colas and most processed foods are also high in phosphorus and should be limited or avoided. It is important to check for the phosphorus content in additives or preservatives, as this inorganic phosphorus is completely absorbed (Ritz, Hahn, Ketteler, Kuhlmann, & Mann, 2012) The calcium recommendation is to maintain intake at 2 grams/day from both dietary and medication sources (Beto et al., 2014). Research suggests that despite the nutrition counseling provided for this population, the adherence to the diet and fluid recommendations is fairly poor and is associated to the emotional challenge of making sense of renal diet information (Beerendrakumar, Ramamoorthy, & Haridasan, 2018; Lambert, Mansfield, & Mullan, 2018).

Nutrition education intervention for CKD and mineral bone disorder

Although the etiology of chronic kidney disease is multifactorial, treatment does not change. The stage of CKD will determine the parameters to be monitored and will help determine the nutrition intervention needed to delay the progression of the disease. Pre-dialysis medical nutrition therapy counseling has been shown to delay the progression of the disease, as well decrease mortality after the first year following initiation of renal replacement therapy (Beto et al., 2014). The nutrition care process algorithm from the Academy of Nutrition and Dietetics' CKD evidence-based literature recommends patients in stages 3 and 4 visit a registered dietitian every 1-3 months for at least 2 hours/month for up to a year (Beto et al., 2014). The amount of nutrition education provided needs to be tailored to the individual needs of the patients.

In a study by Karavetian and Ghaddar (2012), the appropriate amount of nutrition education provided by a well-trained dietitian can impact the overall clinical outcomes and help overcome the barriers leading to the lack of adherence to dietary recommendations often observed in CKD patients. Results from a study by Karavetian et al. (2016) support these findings highlighting the increased need for tailored counseling techniques and nutrition education in this population.

Other studies by Karavetian et al. (2014) demonstrated the impact of increasing the intensity of the protocol used to deliver nutrition education to CKD dialysis patients on clinical outcomes, such as phosphorus control. They measured changes by comparing the improvement in overall outcomes preceding nutrition

education at different degrees of intensity, therefore emphasizing the need for dedicated dietitians as well as stage-based education for this population (Karavetian et al, 2014). Some researchers incorporated the use of questionnaires to assess patient knowledge and quality of life following a structured nutrition education program and also found that a more structured and intense nutrition education program was the most effective in improving patient knowledge and quality of life. With the use validated questionnaires, researchers found that the mean score of patients' knowledge and quality of life in the experimental group receiving intense nutrition education had a significant improvement (Ebrahimi et al., 2016). An important factor to consider when delivering nutrition education is that limited health literacy can impact the quality of life and overall clinical outcomes of ESRD patients (Cavanaugh et al., 2010).

A large percentage of current studies on nutrition education for CKD-BMD focus on the adherence to low phosphorus diets because findings show that hemodialysis patients are less likely to follow phosphorus modifications than potassium and sodium modifications. A study by Duff and Chawke (2017) found that providing information in regards to possible complications of elevated phosphorus when delivering phosphorus focused nutrition education had a significant impact on phosphate levels and patient knowledge (test scores improved by 10%).

Balancing protein and phosphorus intake can be a challenge for CKD patients whether they are using hemodialysis or not. Shifting from a diet consisting mainly of

animal protein to a diet consisting of 70% proteins from plants is an efficient way to lower phosphorus excretion while maintaining optimal dietary intake of protein (Moorthi et al., 2014). Phosphorus in plant-based products is bound to a compound called phytate. Humans lack the enzyme to break down phytate bond phosphorus, leading to low absorption and bioavailability of phosphorus from plant-based sources. Nevertheless, longer observation periods are needed to get a well-rounded understanding of the potential benefits of increased amount of plant-based products on mineral metabolism and cardiovascular complications observed in CKD patients.

Kidney friendly diets- Is it time to re-evaluate?

Whether the current renal diet is effective at providing optimal nutritional status that will not only protect the kidneys but also the heart, is in question. Considering that that an overwhelming percentage of the CKD population dies prior to reaching ESRD due to unforeseen cardiovascular events (Kuro-O, 2011; United States Renal Data System, 2018), this should be an area of focus when dealing with CKD patients regardless of the stage. As previously mentioned, studies suggest that phosphorus may play a role in the manifestation of cardiovascular complications in early stages of CKD despite the normal serum levels, however there is a lack of nutrition focused long-term outcome research to prove this relationship. There are numerous diets with the potential to be effective at delaying the progression of CKD, such as the Mediterranean Diet (De Lorenzo et al., 2010; Smyth et al., 2016) or Dietary Approaches to Stop Hypertension (DASH) diet (Smyth et al., 2016; Tyson et

al., 2016). Although, these diets provide promising results in early stages of CKD when certain micronutrients are not restricted, they are ineffective when patients reach kidney failure. Thus, modifying these diets to decrease the phosphorus load on nephrons at early stages may amplify its potential to delay the disease.

Another aspect of the renal diet currently gaining popularity is its effect on the gut microbiota. Current CKD guidelines do not support a healthy microbiota but tends to support a state of symbiosis that leads to overgrowth of bacteria resulting in the formation of additional uremic toxins (Hasegawa, Jao, & Inagi, 2017; Mohanty, Misra, Mohapatra, & Sahu, 2018). Pairing this with the oxidative stress caused by this state of uremia, not only causes a cyclic relation injuring the kidney even further but it contributes to the endothelial dysfunction and vascular calcification that arises early in the progression of CKD.

Rather than focusing on potential benefits of specific nutrients, upcoming studies should attempt to create a wholesome diet including various novel aspects currently being studied. For example, include gut health in relation to probiotics/prebiotics (Mohanty et al., 2018), antioxidant and anti-inflammatory properties, differences in metabolites of specific types of macronutrient metabolism (ex: saturated vs. unsaturated fatty acids) (Hasegawa et al., 2017) while providing not only nutritional but psychological support. Due to the expected intensity and difficulty maintaining adherence, trials should be conducted in a well-controlled setting and

patients ability and desire to adhere should be considered, since this currently represents the biggest barrier to achieving optimal results.

Perceived Barriers for Achieving Improved Clinical Outcomes

Barriers experienced by renal patients

Despite the number of barriers experienced by both renal patients and renal practitioners, the literature agrees upon the importance of patient education and its impact in clinical outcomes (Narva, Norton, & Boulware, 2016). Many people suffering with chronic kidney disease have low awareness of their health status and may interpret this as a consequence of limited availability of CKD information. According to data from NHANES 1999-2012, the overall awareness of disease status among individuals suffering from CKD is 6.4% (Narva et al., 2016).Unfortunately, many CKD patients lack motivation and readiness to learn, and their limited health literacy only complicates this further (Narva et al., 2016; Umeukeje et al., 2015). Findings indicate that low self-motivation is associated with low adherence to treatment regimen, but unfortunately, there is scarce research on ways to overcome emotional barriers associate with progression to ESRD (Umeukeje et al., 2015). Studies exploring the benefits of peer support suggest that both patients and care givers find peer support helpful, giving them a sense of control and empowerment, reducing the uncertainty of the progression of the disease, and making them feel understood, accepted and less isolated (Taylor, Gutteridge, & Willis, 2015). Experiencing poor continuity of care, not feeling well and having trouble with dietary

and fluid restrictions are also common patient barriers in the treatment of CKD (Lo et al., 2017).

Barriers experienced by renal practitioners

Healthcare providers also have barriers to overcome to effectively treat CKD. Some of the reported barriers include lack of time with patients, difficulty evaluating public awareness, lack of knowledge in at risk population and patients' low literacy levels (Narva et al., 2016). Dietitians report a lack time to give hemodialysis patients a well-rounded education that focuses on improving their knowledge and therefore their adherence to recommendations (Hand & Burrowes, 2015; Stevenson, Tong, Campbell, Craig, & Lee, 2018). Research states that nephrologists also report not having adequate time to properly prepare patients for dialysis or build a relationship with them which makes it more difficult to explain the mechanism of the disease and assess patient knowledge. Many primary care doctors (non-kidney specialist) report to lack confidence in their skills to diagnose, treat and explain CKD to patients (Greer et al., 2015). Lack of education about CKD prior to referral to nephrologist accompanied by late referral from the primary care doctor contribute to the lack of patients' acceptance and trust, as well as the developed fear of dialysis (Greer et al., 2015).

Future Directions

Depression is a frequent comorbidity most often observed among patients in end stage renal disease. There is little evidence on the efficacy of screening tools for depression among this population, therefore despite its elevated prevalence, it is often

overseen (Farrokhi, Beanlands, Logan, Kurdyak, & Jassal, 2017). Research suggests that patient barriers to seek treatment include concern of possible side effects of medications, adding more medications to their already overwhelming regimen, inaccurate perception of severity of problem, risk for depression, and distrust in the efficacy of treatment (Farrokhi et al., 2017). This population may have a negative way of coping, and this decreases adherence to treatment (Farrokhi et al., 2017) .

Multidisciplinary team approach can facilitate the delivery of nutrition interventions, but the disjointed advice that is often given across disciplines is leading to further confusion in patients. Nutritional issues are being addressed differently between disciplines due to the conflicting guidelines or providing advice based on out-of-date literature or inconclusive research. This results in distrust in the efficacy of nutritional treatment (Stevenson et al., 2018). Nephrologists and nurses reported to address nutritional problems for the purpose at hand, meaning that they handle the issue once a complication arises. Dietitians adopt gradual methods of counseling providing individualized support to manage nutritional issues before any medical complications arise (Stevenson et al., 2018). A study on the multidisciplinary team approach found that an integrated action plan was associated with slower decline in GFR over time and decreasing number of patients starting dialysis (Bayliss, Bhardwaja, Ross, Beck, & Lanese, 2011).There is limited research on the use of standardized multidisciplinary approach in the treatment of CKD with implementation of psychological testing to screen for depression, considering the significant effects it

can have on motivation, adherence and overall clinical outcomes (Farrokhi et al., 2017; Taylor, Taylor, Baharani, Nicholas, & Combes, 2016).

Another area in need of further research is the impact of magnesium in clinical outcomes of patients undergoing dialysis. Hypomagnesemia is a common condition among CKD patients due to tubular injuries that lead to magnesium wasting (Oka et al., 2018). Research suggest that lower serum magnesium is a significant predictor of mortality among dialysis patients independent of cardiovascular status and increasing dialysate magnesium has been associate with decreased predisposition to calcification in hemodialysis patients (Oka et al., 2018). Also, the consumption of proton pump inhibitors, a commonly used medication among renal patients for gastroesophageal reflux disease, has been linked to decreased levels of magnesium among CKD population (Alhosaini et al., 2014; Hughes, Chiu, Kalra, & Green, 2018). Intervention studies are needed to explore toxicities associated with magnesium supplementation and to test for optimal strategy for restoration of this electrolyte imbalance.

Summary

According to the United States Renal Data System (USRDS) Annual Report, the prevalence of CKD has increased from 14.2% (NHANES 2001-2004) to 14.8% (NHANES 2013-2016); and the prevalence of ESRD has continued to rise about 20,000 cases per year since 2016 (United States Renal Data System, 2018). This increase can be attributed to increased rates of uncontrolled diabetes and hypertension in our population. The epidemic of chronic kidney disease is associated with higher

mortality rates, thus tailored interventions to delay or stop the progression of the disease are of critical need. The progression of CKD is gradual and although changes in bone mineral biomarkers are not observed until later stages of the disease, early intervention can result in delayed progression. Current nutrition education studies have demonstrated the efficacy of structured and intense nutrition education programs in CKD patient's clinical outcomes, yet there is a lack of work demonstrating the impact of an integrated interdisciplinary approach to nutrition intervention for CKD patients, particularly those undergoing dialysis.

It is of importance to determine the current barriers experienced not only by dietitians and patients but by other renal practitioners in the effort to manage CKD and CKD-MBD through nutrition interventions. Although dietitians are the experts in the field and should be the ones leading the delivery nutrition intervention programs, other members of the renal department should also be well educated in need for dietary modifications and consequences related to poor adherence in order to provide efficient education and accurate information when the time is appropriate. Information delivered should be based on updated evidence-based guidelines. There is a need for ongoing nutrition educational programs for employees from various disciplines dealing with this population to improve the delivery and consistency of nutritional advice across all disciplines.

Despite the favorable outcomes reported in some studies in the literature, mortality rates for CKD have yet to improve. The study hypothesis is that this lack of

improvement is in fact related to the lack of cardiovascular protection provided by the current guidelines and this may be attributed to the lack of optimal nutrient intake, including antioxidant, probiotics/prebiotics and anti-inflammatory food items. The current study was designed to identify the top barriers experienced by renal practitioners. Additionally, the study aimed to identify the most frequently used tools when providing nutrition education to CKD hemodialysis patients. Furthermore, the study seeks to understand specific nutrients being targeted and determine the average amount of time that is currently being devoted to nutrition education in a hemodialysis setting across disciplines.

CHAPTER III

RESEARCH ARTICLE

Hemodialysis care staff perceptions on barriers to optimal health: Results from a qualitative study and national survey

Key words: Qualitative research, cardiovascular disease, chronic kidney disease, mineral and bone disorder, hemodialysis

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Introduction

The obesity pandemic has brought an increased prevalence of chronic diseases, such as type II diabetes mellitus, hypertension, and chronic kidney disease (CKD) (Hruby & Hu, 2015; Hossain, Kawar, & El Nahas, 2007; Hurt, Kulisek, Buchanan, & McClave, 2010; Mitchell, Catenacci, Wyatt, & Hill, 2011). Kidney disease, which represents the ninth leading cause of death in the US (Xu et al., 2018), is a degenerative condition characterized by a gradual decline in kidney function and structural changes; it is classified as CKD when these abnormalities persist for longer than three months, (Kidney Disease Improving Global Outcomes, 2013). CKD is asymptomatic, thus early screening and detection, as well as adherence to prescribed interventions are crucial (National Kidney Foundation, 2019b). Current nutritional guidelines for the CKD are focused on improving the state of uremia observed in this population, however they are not effective at providing the cardiovascular protection this population is in desperate need for as guidelines focus more on restrictions of specific nutrients as opposed to the potential impact of quality over quantity of nutrient intake.

The intervention prescribed following a CKD diagnosis depends on the severity of the disease at the time of detection but it generally includes diet modification, prescription of pharmaceuticals and at later stages, dialysis or kidney transplantation. Regardless of etiology, the loss of kidney function in CKD disrupts

homeostasis in the body. The albumin creatinine ratio (ACR) and the eGFR are mechanisms used to grade the stage of CKD. ACR varies among the stages of CKD. Estimated GFR is a measure used to describe the flow rate of filtered fluid through the kidney (Table 1). When the eGFR is less than 60 mL/min/1.73 m^2, certain disruptions in homeostasis begin to occur. Phosphorus retention occurs due to reduced urinary phosphorus excretion resulting in decreases in serum calcium levels. PTH attempts to restore calcium homeostasis by mobilizing calcium from bone and stimulating renal tubule reabsorption of calcium. PTH also decreases renal phosphorus reabsorption and increases excretion. Thus, serum calcium and phosphorus return to normal at the expense of a higher serum PTH. With every decrease in eGFR, the process repeats itself. Eventually the eGFR gets so low that hyperphosphatemia and hypocalcemia ensue while PTH continues to rise (Martin & Gonzalez, 2007).

Further damage to the bone is caused by a decreased synthesis of $1,25(OH)_2$ vitamin D_3, increased serum phosphorus. The metabolic acidosis that develops due to the failing kidneys contribute to the weakening of the bones. Thus, the combination of bone reabsorption from too much PTH, the buffering of hydrogen ions, and the decreased bone formation due to low $1,25(OH)_2$ vitamin D_3, results in the development of renal osteodystrophy, the bone malformation aspect of CKD-MBD (Martin & Gonzalez, 2007).

It is known that when calcium-phosphorus product exceeds the solubility product, it may contribute to crystal precipitation in the vasculature (Yamada &

Giachelli, 2016). However, klotho and FGF23 are also thought to play a key role in vascular calcification. There is growing evidence gathered from animal experiments that demonstrates that a decrease in klotho levels can cause vascular calcification, cardiac hypertrophy, cardiac fibrosis (Lu & Hu, 2016). A study by Chen et al. (2018) examined the mechanism of phosphate-induced calcification in vascular smooth muscle cells and results suggested that klotho and FGF23 have the capability of reversing the calcification induced by high phosphate intake and suppressing phosphate-induced vascular calcification by inhibiting Wnt7b/β-catenin pathway (Chen et al., 2019). The changes in metabolic pathways of bone minerals, the interruption in calcium and phosphate homeostasis, and the vascular calcification observed in CKD patients in relation to these alterations are collectively known as chronic kidney disease-mineral bone disorder (CKD-MBD) (Kidney Disease Improving Global Outcomes, 2017)

Mineral and bone disorders are an inevitable consequence of CKD. While many approaches are taken to treat CKD-MBD, no data currently exists stating its exact prevalence. Research has shown that intervention in the form of intense nutrition education can significantly improve clinical outcomes as well as improve quality of life (Duff & Chawke, 2017; Ebrahimi et al., 2016; Karavetian et al., 2015, 2016).

Specific Aims

The focus of this study is to distinguish between the different strategies used to treat Chronic Kidney Disease- Mineral Bone Disorder, the perceptions across

disciplines and barriers to maintaining mineral homeostasis during dialysis. The specific aims for this study are: to explore the current barriers perceived by renal practitioners at dialysis units when addressing the imbalance of minerals that manifests as a result of CKD; to identify the nutrition education techniques that are used most frequently in dialysis units and the main concepts discussed in reference to bone mineral metabolism; and to understand what specific nutrients healthcare practitioners target when providing nutrition education to manage CKD-MBD.

Methods

Study Design

This was a descriptive study using the survey method. This study was conducted from February 5th, 2019 to March 21st, 2019. Surveys were distributed to 250 randomly chosen inpatient and outpatient hemodialysis centers in the continental United States. The study was reviewed by the institutional review board at Winthrop University and informed consent was provided prior to the start of the survey by selecting "I agree" on the electronic survey. None of the participants who opened the survey refused to give consent.

Participants and Setting

The participants included in the study were defined as health care practitioners with a registered credential, including any relevant heath care professionals involved in inpatient or outpatient hemodialysis care such as Registered Dietitians, Registered Nurses and Certified Nurse Assistants. In order to maintain confidentiality, certain

demographic characteristics were not obtained. Participants were recruited using the convenience random sampling. Using the USDialysisFinder.com website, a list of 6,027 dialysis centers located in the continental United States were identified, and two hundred and fifty were randomly chosen to be contacted. If the facility agreed to participate, an email was sent containing the link to the electronic survey. Due to low response rate, dietitians were identified through the Renal Practice Group affiliated with the Academy of Nutrition and Dietetics and a blast email was sent to all renal dietitians whose information was available to the public. The state chapters of Academy of Nutrition and Dietetics were also contacted for additional disbursement.

Tools and Instruments

The tool used to gather information was an electronic survey. The questions were designed to provide the following information specific to Chronic Kidney Disease-Mineral and Bone Disorder: how much time is spent with patients working on nutrition education, what nutrients are being targeted during nutrition education, specific nutrition education tools used and current barriers regarding compliance. The survey was reviewed by a renal dietitian from Fort Mill Fresenius Medical Center and the Human Nutrition Program Director at Winthrop University for content validity. The software Qualtrics was used to develop and distribute the survey.

Procedures

Once the clinics agreed to participate in the study, the link to the survey was sent to the participants via email. The potential participants from the Renal Practice

Group were provide with a short introduction in the e-mail that resembled the information from the script followed for the calls to invite them to participate in the graduate thesis project. After providing their consent, participants completed the 18-question survey via Qualtrics.

Statistical Analysis

The study included 76 participants in the renal field, from the continental United States. Of the 76 participants, one was excluded due to participating in the pilot study conducted. Although all participants worked in the renal field, six participants were excluded from the study due to not working with hemodialysis patients. As a result, a total of 68 participants were included in the statistical analysis. Statistical tests, such as chi-square, failed to provide significant results and therefore the descriptive statistics were presented using proportions and graphical methods. Descriptive data was analyzed using the statistical software Minitab and the Microsoft Excel was used to create visual representation of the responses.

Results

Participant and Patient Characteristics

The sample included Registered Dietitians (n=63), Registered Nurses (n=3) and Certified Nurse Assistants (n=2) (Table 3) with 0.5-35 years of experience in the renal field (Figure 3). Their work setting was defined as either in-patient (n=11), out-patient (n=49) or a mixture of both (n=8), and their location was broken down into two region: West (n=15) and East (n=53) (Table 3).

Table 3. Sample demographics

	Registered Dietitian	Registered Nurse	Certified Nurse Assistant
N=	63	3	2
Mean Longevity (yrs. +/- SD)	11.04 +/- 8.26	11 +/- 1.41	4.67 +/-
Eastern U.S. Location	N= 48 (76.2%)	N= 3 (100%)	N= 2 (100%)
Western U.S. Location	N= 15 (23.8%)	N= 0 (0%)	N= 0 (0%)
In-patient Setting	N= 7	N= 3 (100%)	N=1 (50%)
Out-patient Setting	N= 48	N= 0 (0%)	N=1 (50%)
Both (In/Out Patient)	N= 8	N= 0 (0%)	N= 0 (0%)

**Appendix C: Classifies East vs. West U.S. Regions*

Participants were asked to give an estimate of the age range in which most of their patients fall in as well as an approximate percentage of their racial breakdown. Results indicate that the vast majority of patients are ≥ 40 years old (n=64) (Table 4) and most are either White Caucasian (mean 40.28 +/- 24.24) or African American (mean 42.30 +/- 27.93).

Patient Age Range	N=
0-18 years old	2 (3%)
20-40 years old	2 (3%)
40-60 years old	32 (47%)
>60 years old	32 (47%)

Table 4. Breakdown of patient age

Nutrition Education

Participants were asked the amount of years that they have been working in direct patient care of CKD clientele, average age range of CKD patients, average percentage of CKD patients receiving nutrition education specific to CKD, average amount of time spend on nutrition education with each patient per visit and at what stage of CKD do they believe to be the most critical to begin nutrition intervention to effectively treat CKD-MBD. Graphics were used to give a visual break down of the data.

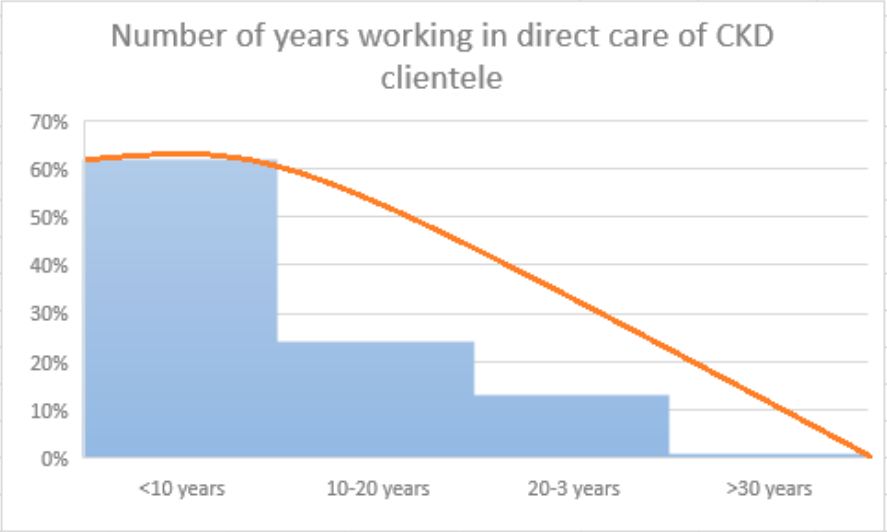

Figure 5. Number of years working in direct care of CKD clientele
**Percent is calculated within all data*

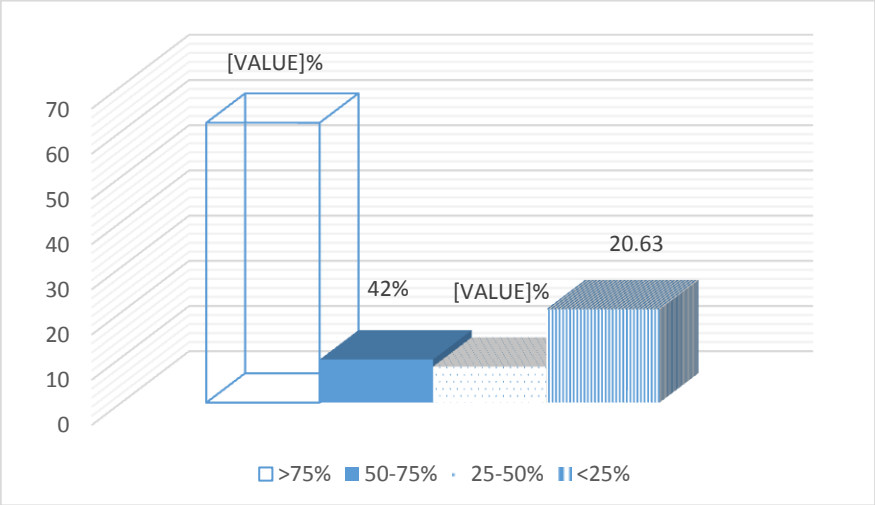

Figure 6. Percentage of renal patients receiving nutrition education specific to CKD

**Percent is calculated within all data*

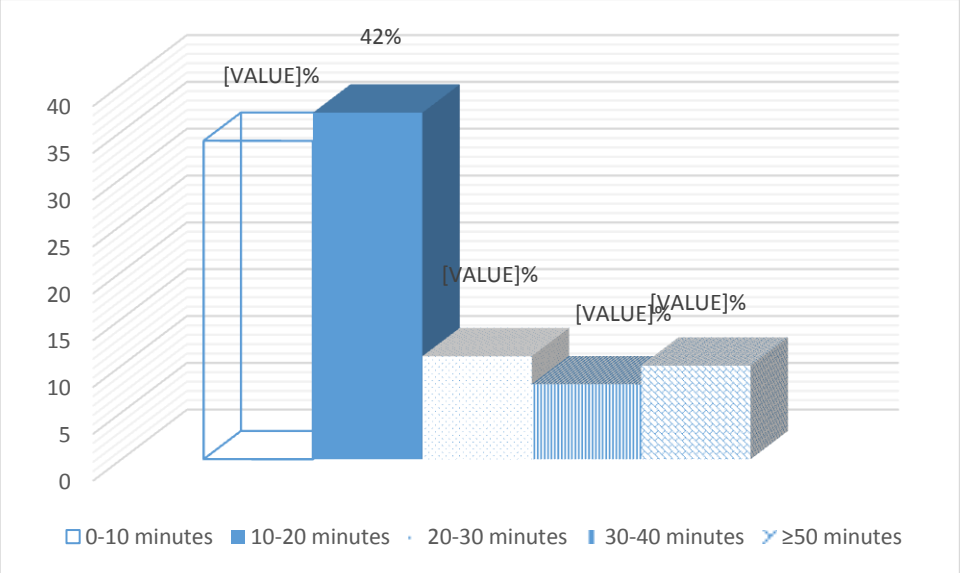

Figure 7. Average amount of time spent on nutrition education with each patient per visit

**Percent is calculated within all data*

Participants were also asked to rank the three most important tools used to aid in nutrition education and three most important micro- and macro-nutrients when educating CKD patients. Graphics were used to summarize the results.

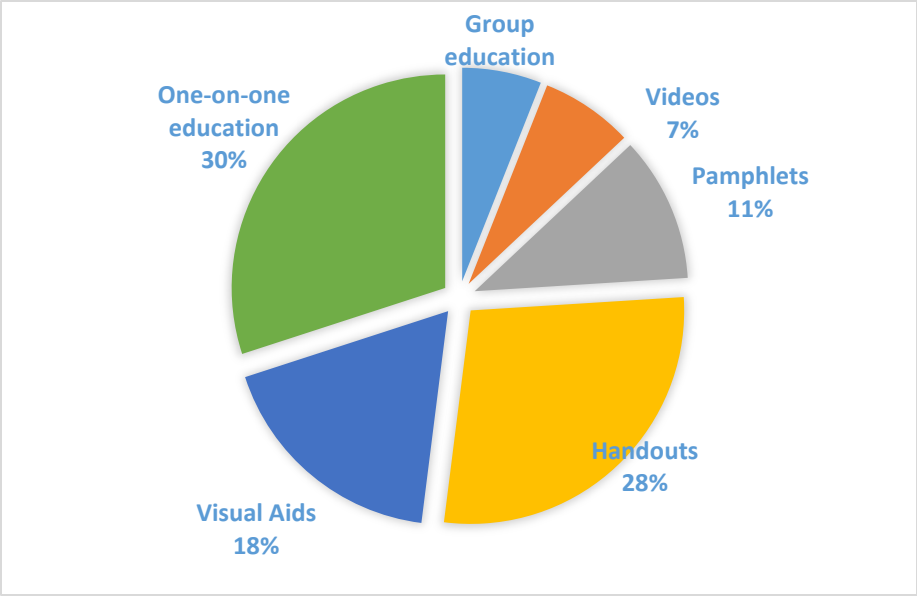

Figure 8. Tools ranked as one of the three most important used in nutrition education
**Percent is calculated within all data*

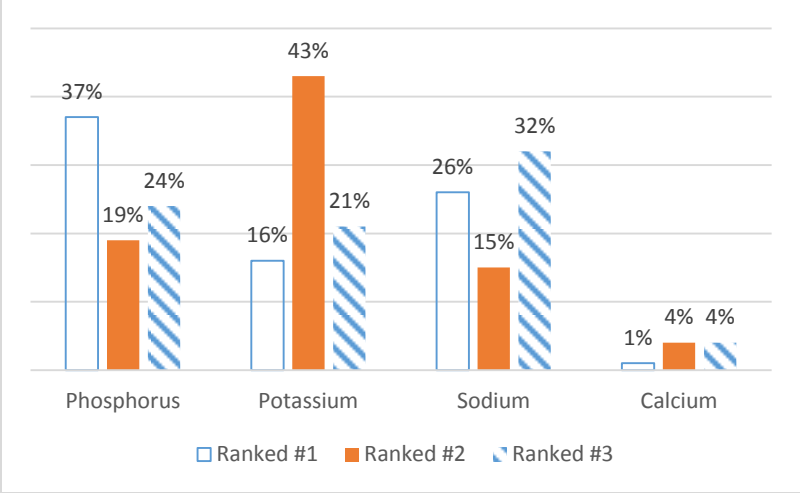

Figure 9. Three most important micronutrients for CKD nutrition education
**Percent is calculated within all data*

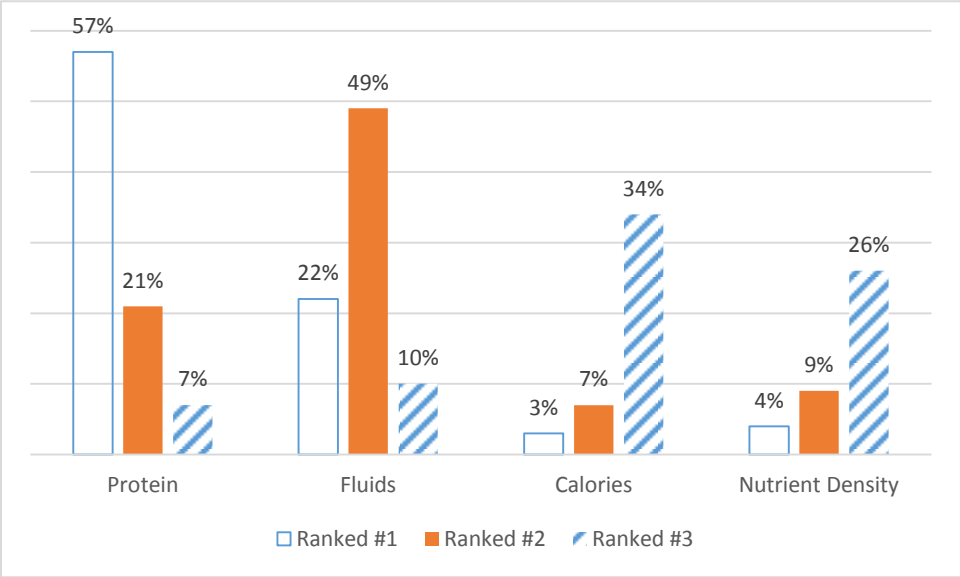

Figure 10. Three most important macronutrients for CKD nutrition education
**Percent is calculated within all data*

Barriers in managing CKD in hemodialysis patients

It is important to keep in mind that the barriers to compliance assessed were identified from the renal practitioner's perspective rather than patient perspective. To assess common beliefs around nutrition education and CKD-MBD, there was a question on whether or not they believe that nutrition education is an effective method of treatment and, if so, what stage they found to be most critical to implement the nutrition intervention. The results showed that only one out of 68 participants did not find nutrition education to be an effective methods and close to half (n=33) of the participants believe that nutrition should be initiated at early stages (stage one or two) versus late stages (stages three-five) (n=35).

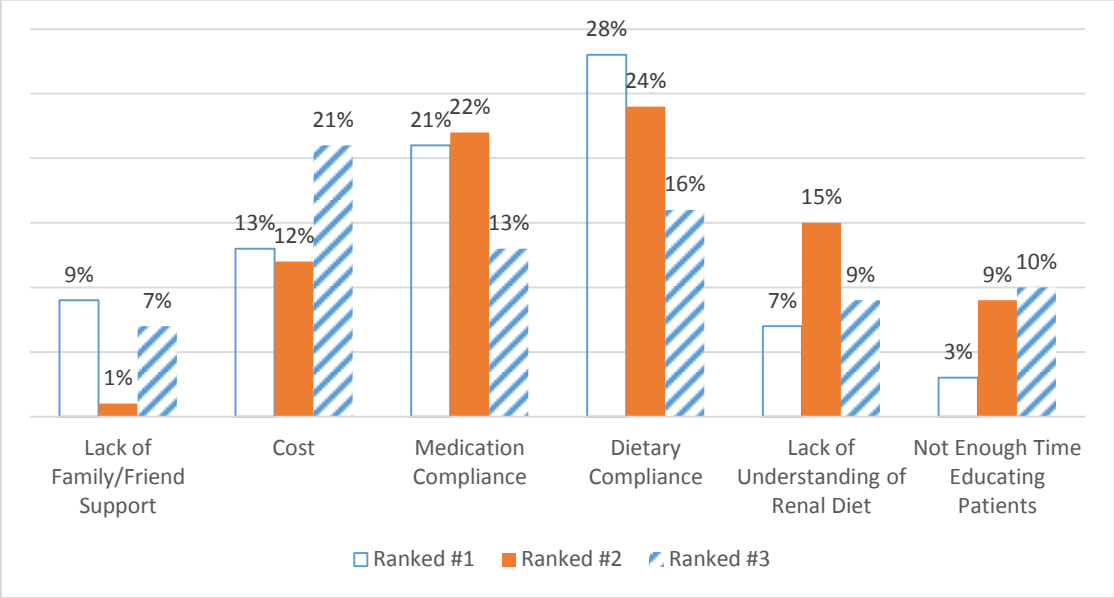

Figure 11. Barriers in managing CKD in hemodialysis patients
**Percent is calculated within all data*

Discussion

The findings of this study suggest that there is a lack of focus on the quality over the quantity of nutrients when providing nutrition education. This may lead to suboptimal nutrient intake in a large portion of the CKD population. When asked to rank macronutrient topics in order of importance, nutrient density was not chosen as one of the top three most important macronutrient topics. Despite efforts to improve CKD patients' quality of life, the results of this lack of focus on the nutrient density translates into the negative outcomes commonly observed in relation to cardiovascular health and subsequent mortality rates. Not every recommendation is quantifiable when dealing with CKD patients.

Findings from other studies have demonstrated a positive impact on clinical outcomes by increasing the intensity of the protocol used to deliver nutrition education to CKD dialysis patients (Karavetian et al., 2016). Yet dietitians have reported a lack of time to give patients a well-rounded education that focuses on improving knowledge and adherence to recommendation (Hand & Burrowes, 2015). This study's results support previous findings by showing that the vast majority of dietitian in hemodialysis units spend (N=52) only from 0-20 minutes giving nutrition education to each patient per visit, in spite of renal practitioners reporting that >75% of their patients receive nutrition education specific to CKD. There was not a significant difference reported between in-patient and out-patient setting, or between the West and East region of U.S when it came to the time spent educating patients. Taking into account the limited patient awareness, low literacy rates, and lack of education prior to advanced stages of CKD that has been reported by previous data, the reported time frame seems insufficient. Another aspect to consider is that a reported 94% of patients are older than 40 years old, which can sometimes make it more difficult for change to occur. Although findings from this study did not identify "not enough time educating patients" as a top barrier in managing CKD in hemodialysis units, it was ranked as number one barrier by nine percent of participants, following the barriers of cost, medication compliance, and dietary compliance, making it a significant challenge when trying to improve overall patient outcomes.

To my knowledge, there are no studies exploring at which stage renal practitioners consider to be most critical to initiate nutrition education. Interestingly,

results from this data showed that about half of the participants considered early stages (stages 1 and 2), with the other half considering late stages (stages 3 to 5) to be the most critical for initiation of nutrition intervention.

Aside from the need for further research on ways to detect and treat CKD more effectively at earlier stages of the disease, the comorbidity of depression should also be given closer attention. Further research should study how a multidisciplinary approach, including implementation of improved psychological testing to screen for depression could impact the mortality rate of dialysis patients.

Conclusion

Although dialysis is meant to hold the role of an "artificial kidney", it is not as effective at removing waste products as are the kidney when in a healthy state. When paired with an appropriate diet, medications and patient compliance, patient outcomes have shown to improve. However, the overall mortality rate and cardiovascular complications often experienced by this population have not gotten better, and this may be attributed to lack of concentration in the quality of the recommended diet. Current guidelines are targeting the state of uremia in dialysis patients and quantity of nutrient intake is given more importance than the actual quality, leading to a harmful state for these patients' cardiovascular system. This study identified cost, medication and dietary compliance as the top barriers for managing CKD and concluded that one-on-one education is the most effective tool used in nutrition intervention. Participants consider phosphorus, potassium and sodium to be the most important micronutrients

for CKD dialysis patients, yet if the focus was given to the overall quality of the diet, phosphorus and sodium would not be micronutrients of concerns. Dietary recommendation for this population should be individualized taking into consideration the etiology of each patient's kidney condition. This will require more time devoted to patient knowledge, tailored dietary interventions and an interdisciplinary approach including the help of a mental health professional. As complex as CKD can get, the regimen has to be just as aggressive.

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WINTHROP UNIVERSITY

Sponsored Programs and Research

IRB PROTOCOL #:	IRB19087R
TITLE OF PROJECT:	Chronic Kidney Disease-Renal Osteodystrophy
RESEARCHER OF RECORD:	Daniela Gutierrez
FACULTY ADVISOR:	Hope Lima
EXEMPTION DATE:	11/14/2018
EXEMPTION CATEGORY:	14(b) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior unless (a) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (b) any disclosure of the human subjects' responses outside the research could reasonably place the subject at risk of criminal or civil liability or be damaging to the subjects' financial standing , employability or reputation. [45CFR46(b)(2)] Research involving children (subjects who have not attained the age of 18 years) is not exempt unless the research involves only the observation of public behavior and the researchers do not participate or impact the activities being observed. [45CFR46.401(b)]

The Request for Review of Research Involving Human Subjects identified above has been reviewed by the Winthrop University Institutional Review Board (IRB) and has been determined to be exempt from IRB review. You may begin your research on or after the Exemption date show above.

A waiver of obtaining signed informed consent has also been granted. This waiver means the participant is not required to sign the informed consent document, but you must still advise the participants of the purpose of the research, their rights as a research subject and any risks or benefits associated with participating in the research.

A *Request for Modification of Previously Approved or Exempt Protocol* must be completed by the researcher and submitted to the IRB for review for any proposed changes or modifications to the protocol. IRB approval must be received prior to amended changes or modifications being implemented by the researcher. These changes may include a change in a survey instrument, the addition or deletion of a research site, a change in personnel, a change in methodology or a change in the Researcher of Record.

Use the form *Adverse Event Report* to report any negative consequences that occur as a result of participation in a research project. . An "adverse event" or "adverse experience" is an undesirable and unintended, though not necessarily unanticipated, injury or physical or emotional consequence to a human subject. "Unanticipated Problems" may or may not include specific events experienced by individual subjects, but are developments within the research activity that suggest a potential for increased risks to subjects or others.

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WINTHROP UNIVERSITY

Grants and Sponsored Research Development

IRB Protocol #:	IRB19087RM2
Project Title:	Chronic Kidney Disease-Mineral Bone Disorder
Researcher of Record:	Daniela Gutierrez
Faculty Advisor:	Hope Lima
Exemption Date:	11/14/2018
Modification Approval Date:	1/24/2019
Exemption Status:	Exempt under 45CFR46(b)(2)

The Protocol and the Request for Modification identified above has been reviewed by the Chair of the Winthrop University Institutional Review Board (IRB) and continues to qualify as exempt from IRB review.

A *Request for Modification of Previously Approved or Exempt Protocol* must be completed by the researcher and submitted to the IRB for review for any further proposed changes or modifications to the approved protocol. IRB approval must be received prior to amended changes or modifications being implemented by the researcher. These changes may include a change in a survey instrument, the addition or deletion of a research site, a change in personnel, a change in methodology or a change in the Researcher of Record.

Use the form *Adverse Event Report* to report any negative consequences that occur as a result of participation in a research project. An "adverse event" or "adverse experience" is an undesirable and unintended, though not necessarily unanticipated, injury or physical or emotional consequence to a human subject. "Unanticipated Problems" may or may not include specific events experienced by individual subjects, but are developments within the research activity that suggest a potential for increased risks to subjects or others.

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Sample Email:

Subject: Chronic Kidney Disease-Mineral Bone Disorder Survey

To Whom It May Concern:
Thank you for your interest in participating in our research study looking at nutrition education for chronic kidney disease- mineral bone disorder (CKD-MBD). The purpose of this study is to look at the current standards of care in place to treat the progression of CKD-MBD with nutrition education. We would greatly appreciate if you took 10-15 minutes of your time to complete our electronic survey. This survey is intended to get insight of the perspective of renal healthcare practitioners such as registered dietitian, nurse, medical doctor, social worker and /or any relevant health care professional involved in outpatient and inpatient hemodialysis patient care. Your participation is voluntary and will remain confidential. The information gathered will help to determine if further research in the treatment of CKD-MBD with nutrition intervention is necessary. If you decide to participate in this research and change your mind, you may withdraw at any time.

If you have any questions about the research study, please contact Daniela Gutierrez by email: delgadod2@winthrop.edu, or by phone: 704-925-5396.

Dr. Hope Lima supervises this research. You can reach Dr. Lima by email: limah@winthrop.edu or by phone: 803-323-4553 for further questions.

Please click the following link to access the survey:
https://winthropstudents.qualtrics.com/jfe/form/SV_bNGByd8lYiC8Tad

Thank you so much for your participation.

Informed Consent attached to survey:

Chronic Kidney Disease-Mineral Bone Disorder Survey

The purpose of this study is to look at the current standards of care in place to treat the progression of Chronic Kidney Disease-Mineral Bone Disorder with nutrition education and intervention. We would greatly appreciate if you took 10-15 minutes of your time to complete our electronic survey. Your participation is completely voluntary and will remain confidential. All electronic data will be stored on a USB drive and all paper documents containing data will be safeguarded in an envelope kept in a locked cabinet in the Dalton room 304, Winthrop University. The electronic data and paper documents will be destroyed after 3 years or after publication, whichever comes first. To help protect your identity, the surveys will not personally identify you with your responses and any identifiers will be erased before the data is analyzed. There is little to no risk in your participating in this research project. The information gathered will help to determine further research in the treatment of Chronic Kidney Disease-Mineral Bone Disorder with nutrition intervention. If you decide to participate in this research, you may withdraw at any time.

If you have any questions about the research study, please contact Daniela Gutierrez by email: delgadod2@winthrop.edu, or by phone: 704-925-5396.

Dr. Hope Lima supervises this research. You can reach Dr. Lima by email: limah@winthrop.edu or by phone: 803-323-4553 for further questions.

By selecting agree you are consenting to participate in this research study.

a. Agree
b. Disagree

1. Did you participate in the survey development or original pilot study (Renal Osteodystrophy Survey)?
    a. Yes (skip to the end)
    b. No

Healthcare Provider Demographics

2. Do you work with hemodialysis patients?
    a. Yes
    b. No (if no, thank you for your time)

3. In which state of the US do you currently work at?
    a. _____

4. In which setting do you see your patients?
    a. Inpatient
    b. Outpatient
    c. Both
    d. Other:_____

5. What is your role in working with Chronic Kidney Disease patients/clients?
    a. Registered Dietitian/Registered Dietitian Nutritionist
    b. Renal Nurse
    c. Nurse Practitioner
    d. Physician Assistant
    e. Medical Physician
    f. Social Worker
    g. Other (please specify) : _____

6. How long have you been working in direct patient care of Chronic Kidney Disease clientele?
    a. _____

Chronic Kidney Disease Patients' Demographics

7. On average, what age range do the majority of your Chronic Kidney Disease patients fall in?
    a. Under 18 years old (skip to the end)
    b. 20 – 40 years old
    c. 40 – 60 years old
    d. More than 60 years old

8. What is the racial breakdown of the chronic kidney disease patients under your care? (Please provide approximate percentages)
    a. White Caucasian _____
    b. African American_____

c. American Indian _____
d. Asian_____
e. Hispanic / Latino_____
f. Other (please specify:)_____

Nutrition Education for Chronic Kidney Disease

9. Do you believe that nutrition intervention is an effective way to manage Chronic Kidney Disease?
    a. Yes
    b. No (if no, skip to the end)

10. On average, what percentage of your Chronic Kidney Disease patients receive nutrition education specific to CKD?
    a. 0% (if 0%, skip to the end)
    b. less than 25%
    c. 25%-50%
    d. 50%-75%
    e. 75% or more

11. What is the average amount of time that you spend on nutrition education with each patient per visit?
    a. 0-10 minutes
    b. 10-20 minutes
    c. 20-30 minutes
    d. 30-40 minutes
    e. 50 minutes or more

12. Please rank the **three** most important tools you use to aid in your nutrition education with #1 being the most important.
    a. Pamphlets _____
    b. Group education _____
    c. One-on-one education _____
    d. Visual aids _____
    e. Videos _____
    f. Handouts _____

13. Please rank the **three** most important micronutrients included in your nutrition education with Chronic Kidney Disease patients with #1 being the most important.
    a. Sodium _____
    b. Potassium _____
    c. Phosphorus _____
    d. Calcium _____
    e. Other (_____)

14. Please rank the **three** most important macronutrients topic included in your nutrition education with Chronic Kidney Disease patients with #1 being the most important.
    a. Protein _____
    b. Fluids _____
    c. Calories _____
    d. Nutrient Density_____
    e. Other (_____)_____

15. Please rank the **three** biggest barriers in managing Chronic Kidney Disease in hemodialysis patients with #1 being the biggest barrier.
    a. Lack of family/friend support _____
    b. Costs _____
    c. Medication compliance_____
    d. Dietary compliance _____
    e. Lack of understanding of nutrition information provided _____
    f. Lack of time with patients_____
    g. Other (please specify: _____)

16. At what stage of chronic kidney disease do you believe to be the most critical to begin nutrition intervention in the prevention of Chronic Kidney Disease-Mineral Bone Disorder?
    a. Early stages of chronic kidney disease (Stages 1 & 2)
    b. Advanced stages chronic kidney disease (Stages 3 & 4)
    c. End stage renal disease (Stage 5)

17. If you have any further comments regarding this topic please comment here.

Phone Script

“Hello, My name is _____, I am a graduate student in the Human Nutrition program at Winthrop University in Rock Hill, South Carolina. I was wondering if you had a few minutes to discuss if your facility would be willing to participate in a graduate thesis research project.

If YES:

“Great! The purpose of our study is to look at the current standards of care in place to prevent the development of Chronic Kidney Disease-Mineral Bone Disorder with nutrition education and intervention. Participating in our study will require you and your staff to complete a brief survey that will take approximately 10-15 minutes to complete. Would this be of interest to you?

IF NO:

“Thank you so much for your time, have a wonderful day”.

IF YES:

Great, can you please provide the best email address to send a link to the electronic survey to be completed along with the information about how your privacy will be protected (Obtain email).

Thank you. Do you have any questions at this time (Answer any questions). Thank you so much for your interest in our study and have a wonderful day”.

Appendix B. Sample Diet

Breakfast

- 1 medium egg
- 2 medium egg whites
- 1 cup steamed spinach
- 1 slice whole wheat bread
- 1 cup strawberries

Lunch

- 3.5 oz. of chicken breast
- 1 cup whole wheat spaghetti
- 2 tablespoons of homemade pesto
- 1 cup cucumber salad with homemade with 1 tbsp. Italian dressing

Dinner

- 3 oz. New York strip steak with parsley as garnish
- ½ cup Brussel sprouts
- 1.5 cup tossed salad with 1 tbsp. of olive oil and 3 lime wedges
- 1 cup cucumber salad with homemade Italian dressing

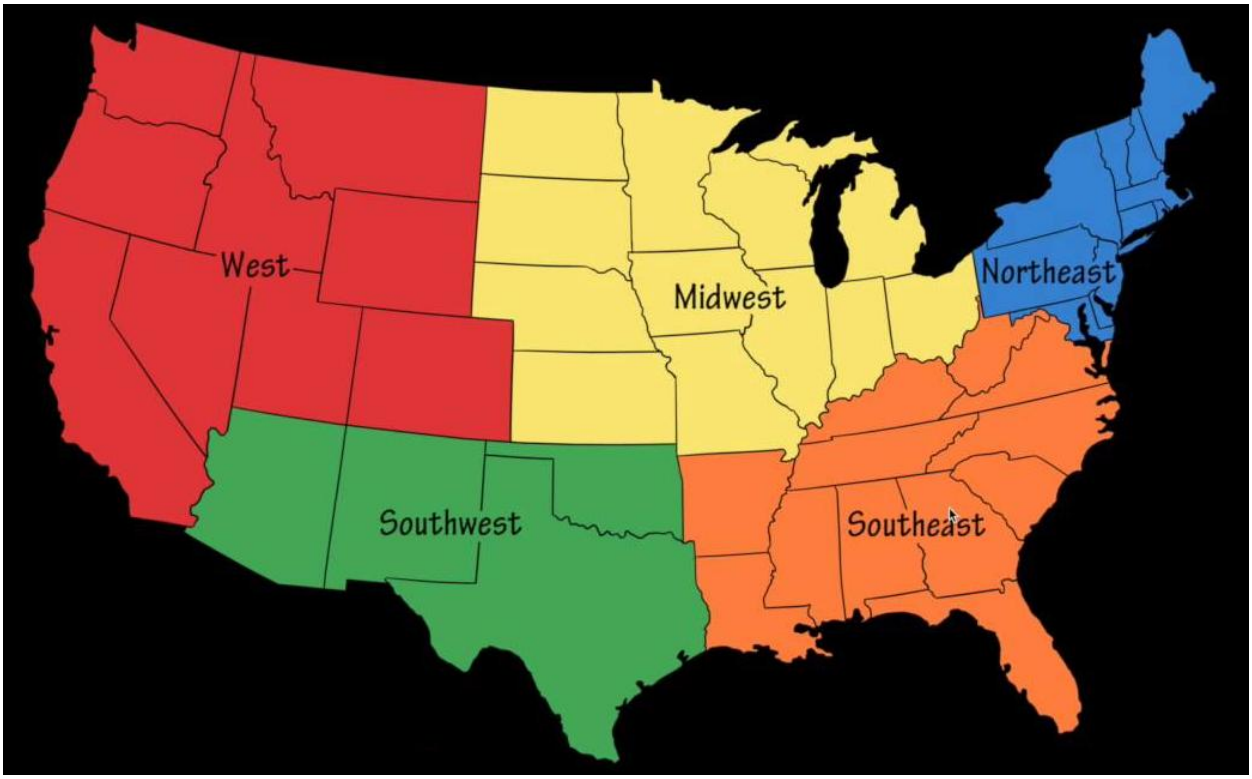
Snacks

- 1 cup Frozen Grapes
- ¾ cup of Blueberries

Nutrient Details	Quantity
CALORIES	1411 calories
PROTEIN	87g
FAT	63.13
CARBS	138.23
Omega 3	1.65g
Iron	12mg
Magnesium	225mg
Calcium	354mg
Phosphorus	766mg
Potassium	2500mg
Vitamin D	43 IU
Cholesterol	241mg
Vitamin K	285.6mcg
Sodium	1050mg

Things to consider: Micronutrient will vary from day to day and you should aim to consume a varied diet to ensure overall optimal consumption. Clients are not expected to reach **all DRI daily. This diet was intended to fit a 1300-1500 kcal plan. This nutrient analysis only takes into consideration sodium from the foods and ideally no salt will be added, however, there is room for variation without exceeding the recommended amount.*

Appendix C. East VS. West U.S. Breakdown



**Originally broken down into 5 regions- only used East vs. West for analysis*